

Answer 1:

Bibliographic Information

Efficacy of anticancer agents in vitro and in vivo using cultured human endometrial carcinoma cells. Study of therapeutic index. Yasui, Yoshie. Sch. Med., Nagoya City Univ., Nagoya, Japan. Nippon Sanka Fujinka Gakkai Zasshi (1987), 39(2), 303-6. CODEN: NISFAY ISSN: 0300-9165. Journal written in English. CAN 106:188338 AN 1987:188338 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Employing the new cell line, NUE-1, which was derived from cells of ascites in a woman with endometrial carcinoma, the sensitivity test for anticancer agents was carried out in culture and xenografts in nude mice. Anticancer activity in vitro was evaluated by counting surviving cells, and the therapeutic index was expressed by LD50 for mice/MLD90 (90% mean LD) in vitro. NUE-1 cells were inoculated s.c. in BALB/c nude mice, and then tumors serially transplanted were used as materials. Anticancer agents (adriamycin (ADM) [23214-92-8], cisplatinum [15663-27-1], chromomycin A3 [7059-24-7], carbazilquinone [24279-91-2], and mitomycin C [50-07-7]) at 1/3 LD50 dosage for mice were administered i.p. on a schedule of 3 doses for every 4 days. The results were as follows: (a) the therapeutic index of ADM was highest at 5-19 times the others; (b) in vivo, ADM demonstrated chemotherapeutic effectiveness, whereas the others had no significant effect; and (c) there was a close correlation between the therapeutic index and in vivo anticancer effect using nude mice.

Answer 2:

Bibliographic Information

Antitumor efficacy of seventeen anticancer drugs in human breast cancer xenograft (MX-1) transplanted in nude mice. Inoue, Katsuhiko; Fujimoto, Shuichi; Ogawa, Makoto. Div. Clin. Chemother., Cancer Chemother. Cent., Tokyo, Japan. Cancer Chemotherapy and Pharmacology (1983), 10(3), 182-6. CODEN: CCPHDZ ISSN: 0344-5704. Journal written in English. CAN 99:98704 AN 1983:498704 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activity of 17 anticancer drugs was studied in the treatment of a human breast cancer tumor (MX-1) transplanted into nude mice. The antitumor activity of the drugs was evaluated at the LD10 predetd. in mice as a std. therapeutic dose. Drugs were administered i.v., i.p., or orally, and antitumor activity was assessed by drug-induced growth inhibition measured by calipers. Among the 17 anticancer drugs, the most active compds. (max. inhibition of rate of tumor growth: $\geq 90\%$) are mitomycin C, chromomycin A3, vincristine, vinblastine, vindesine, and hexamethylmelamine. Another group of compds. showed moderate activity (max. inhibition rate of tumor growth: 89%-50%), these being adriamycin, daunomycin, mitoxantrone, bleomycin, 5-fluorouracil, 6-thioguanine, and ftorafur. The remaining 4 drugs (peplomycin, cytosine arabinoside, 6-mercaptopurine, and methotrexate) were inactive against the MX-1 tumor. These results suggest that in the nude mouse-human tumor xenograft system there is a good correlation between the antitumor activity of various anticancer drugs and their clin. efficacy; this system is therefore expected to be a useful model for secondary screening.

Answer 3:

Bibliographic Information

Chemotherapy of yolk sac tumor heterotransplanted to nude mice. Sawada, Masumi; Hayakawa, Kenichi; Matsui, Yoshiaki; Nishiura, Haruhiko; Okudaira, Yoshio. Res. Inst. Microb. Dis., Osaka Univ., Osaka, Japan. Nippon Sanka Fujinka Gakkai Zasshi (1980), 32(10), 1596-602. CODEN: NISFAY ISSN: 0300-9165. Journal written in Japanese. CAN 96:62670 AN 1982:62670 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

adriamycin [23214-92-8] (5 Mg/kg), carbazilquinone [24279-91-2] (0.6 mg/kg), mitomycin C [50-07-7] (0.2 mg/kg), 5-fluorouracil [51-21-8] (25 mg/kg), cyclophosphamide [50-18-0] (20 mg/kg), chromomycin A3 [7059-24-7] (0.05 mg/kg), vinblastine [865-21-4] (1 mg/kg), and bleomycin [11056-06-7] (3 mg/kg) were given i.p. to nude mice bearing human yolk sac tumor; vinblastine in combination with bleomycin produced the most effective antitumor activity. The results of activities were compared with those of clin. studies, and the relations among the drugs, tumor, and hosts are discussed.

Answer 4:

Bibliographic Information

Validated high-throughput screening of drug-like small molecules for inhibitors of ErbB2 transcription. Marx Corina; Berger Crystal; Xu Fan; Amend Cliff; Scott Gary K; Hann Byron; Park John W; Benz Christopher C Program of Cancer and Development Therapeutics, Buck Institute for Age Research, Novato, CA 94945, USA Assay and drug development technologies (2006), 4(3), 273-84. Journal code: 101151468. ISSN:1540-658X. (COMPARATIVE STUDY); (EVALUATION STUDIES); Journal; Article; (JOURNAL ARTICLE); (VALIDATION STUDIES) written in English. PubMed ID 16834533 AN 2006412314 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

A whole cell high-throughput screening assay was developed and tested against > 2,000 structurally and functionally diverse drug-like small molecules to identify lead compounds capable of cell permeability and selective silencing of ErbB2 transcription. Screening employed reporter sublines clonally selected from ErbB2-negative MCF7 breast cancer cells after stable genomic integration of the ErbB2 proximal promoter driving a luciferase reporter; anti-ErbB2 activities (50% inhibitory concentration values) were compared to inhibition of control MCF7 sublines bearing integrated reporters driven by either a mutated ErbB2 promoter or the cyclin D1 promoter. Of the seven resulting lead compounds, four emerged from the National Cancer Institute (NCI)/ Developmental Therapeutics Program (DTP) Structural Diversity Set (NSC-131547, NSC-176328, NSC-259968, and NSC-321237); three others emerged from a panel of anticancer compounds with known mechanistic actions and included a minor groove DNA-binding antibiotic (NSC-58514, chromomycin A3), a hydroxamic acid inhibitor of histone deacetylases (NSC-709238, trichostatin A), and a tripeptide aldehyde proteasome inhibitor (MG-132). For optimization, 58 scaffold analogs of the four NCI/DTP structural leads and nine functional analogs of the mechanistic leads were secondarily screened to identify seven compounds with comparable or superior activity relative to the leads, including an approved anticancer drug, PS-341 (bortezomib). PS-341 activity was validated against cultured ErbB2-positive breast cancer cell lines (SKBr3 and BT474) and a trastuzumab-resistant ErbB2-positive breast cancer xenograft model (B585), in which PS-341 antitumor activity correlated with selective down-regulation of ErbB2 mRNA and protein levels, confirming the ErbB2- silencing potential of proteasome inhibitors.